

Galanin and Neuropeptide Y interaction leads to antidepressant effects through hippocampal cell proliferation.

Manuel Alejandro Narváez Peláez, Ramon Fores-Pons, Mariana Pita-Rodriguez, Kjell Fuxe, Dasiel O. Borroto-Escuela.

Galanin (GAL) interacts with Neuropeptide Y Y1 receptors (NPYY1R) in several regions of the central nervous system associated with mood and motivation, through GAL receptor 2 and NPYY1 receptor 1 (GALR2/NPYY1R) heterodimers. The current work is to evaluate GALR2 and NPYY1R interactions concerning depression-like behavior and newborn cell proliferation in the ventral hippocampal Dentate Gyrus.

Rats (n = 6-8 per group) were randomly assigned to the groups. Each group received i.c.v. injections of artificial Cerebro Spinal Fluid (aCSF), GAL or NPYY1R agonist [Leu31,Pro34]NPY alone or in combination and 24 h later rats were subjected to a 5-min swimming session (test). A different set of rats received ip injections of BrdU 50mg/Kg at 2 and 4 hours after icv injections. 24 hours later brains collected for immunostaining to evaluate cell proliferation.

We observed that the icv injection of GAL and NPYY1R agonist significantly enhanced the decrease in the immobility and the increase in the swimming behavior compared with the NPYY1R agonist alone. Furthermore, GALR2 is involved in this GALR/NPYY1R interaction, since the presence of the GALR2 antagonist M871 counteracted all the parameters. In parallel, coadministration of GAL and NPYY1R agonist increased BrdU-labeled cells located in the SGZ compared with aCSF, GAL and the NPYY1R group.

These results indicate that GALR2/NPYY1R interactions can provide a novel integrative mechanism in depression-related behavior and may give the basis for the development of drugs targeting GALR2/NPYY1R heteroreceptor complexes. Study supported by Proyecto UMA18-FEDERJA-100, Proyecto Puente-Universidad de Málaga, Proyecto Crowdfunding "Más Neuronas, menos depression" Universidad de Málaga